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Response to, "On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith."

A B S T R A C T

It is not true that successive groups of researchers from academia and research institutions—scientists who served on panels of the US National Academy of Sciences (NAS)—were duped into supporting a linear no-threshold model (LNT) by the opinions expressed in the genetic panel section of the 1956 "BEAR I" report. Successor reports had their own views of the LNT model, relying on mouse and human data, not fruit fly data. Nor was the 1956 report biased and corrupted, as has been charged in an article by Edward J. Calabrese in this journal. With or without BEAR I, the LNT model would likely have been accepted in the US for radiation protection purposes in the 1950's.

1. Introduction

I write about an article in volume 142 of the journal, pages 432–442, (Calabrese, 2015), entitled, "On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith." The acerbic title hints at the content that is to follow, namely repeated *ad hominem* attacks on the actions and motives of historical figures, charitable and scientific institutions, including the Rockefeller Foundation, past committees of the US National Academy of Sciences (NAS), especially the 1956 genetics panel report in the first Biological Effects of Atomic Radiation (BEAR-I) report (NAS, 1956), as well as an NAS president, a president of the American Association for the Advancement of Science, and a president of the Rockefeller Institute for Medical Research – all persons and groups who supported the linear non-threshold model of radiation health effects in any way or did not disavow it. In sentence after sentence, the author deviates from norms for scientific research journals, suggesting conspiracies, relying on speculation, and attributing motives and states of mind (see Table 1).

Alarm bells should go off for every reader, when an advocate for a minority theory declares that scientists and institutions are deceitful, complicit, and/or corrupt. The minority theory in this case is radiation "hormesis," which posits that low doses of ionizing radiation have positive health effects.

A key thesis of the article is that successive groups of researchers from academia and research institutions—scientists who served on panels of the NAS—were duped into supporting an LNT or quasi-LNT model by the opinions expressed in a biased and corrupted genetic panel section of the 1956 BEAR I report. As discussed in what follows, I find this extraordinary claim to be based on an incomplete assessment of the historical record, which in contrast indicates that; 1) the BEAR I report's conclusion were not biased when compared to contemporaneous reports prepared for countries other than the US, 2) successive NAS committees actually dismissed the highest quantitative genetic risk estimates of BEAR I, did not rely on Drosophila (fruit fly) data, and had their own views of the LNT model, 3) BEAR I had a negligible impact on subsequent NAS reports starting as early as 1972, and 4), with or without BEAR I, the LNT model would likely have been accepted in the US for radiation protection purposes in the 1950s. In the Appendix, for completeness, I deal with specific charges of corruption and political motivation. I also respond there to suggestions of bias in early fruit fly radiation studies carried out by Curt Stern and collaborators. Additional comments can be found in an unpublished project report (Beyea, 2016).

2. Bias and corruption

If the BEAR I committee were biased and corrupt, it is difficult to explain how other expert groups that the Calabrese article does not discuss came to similar conclusions about the LNT model and quantitative mutation risk. For instance, a detailed, 128-page report from the UK Medical Research Council, prepared by prominent UK scientists, coordinated to appear on the same date as the US BEAR I report (Hamblin, 2007), came to similar conclusions about the LNT model and genetic risks (MRC, 1956). There were some differences in conclusions between the two reports, despite attempts to remove them, but none relevant to the current discussion. For instance, the US panel focused on population genetic risk and recommended cumulative dose limits for populations, not just limits on individual exposure, whereas the UK panel focused on individual genetic risk and made no dose limit recommendations for populations, viewing those as beyond its responsibility. (Hamblin, 2007). Both panels supported the LNT model at low doses. The UK report complements the BEAR I panel's semi-popular report by presenting the underlying citations and logic used by the panel's geneticists in reaching their conclusions about radiation risk.

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Table 1
Examples of pejorative attacks in the article, entitled, "On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith." (Emphasis added).

1	"… personal and professional relationship with Muller that would markedly impact the LNT *deception* story.."
2	"…especially seen through the actions of the NAS BEAR I Genetics Panel in 1956 which assured the acceptance of the LNT by *falsifying and fabricating* the research record, thereby constituting *scientific misconduct at the highest possible level*.."
3	"Stern's unusual behavior makes sense when viewed as an attempt to blunt any challenge to the linear dose–response model (i.e., by demanding that the data of Caspari not be accepted)"
4	"….of the threshold model at the Nobel Prize Lecture was *deceptive* and *not without ideological underpinnings*"
5	"As for Muller, he must have surely felt relief as he was spared the trouble of having to defend his *highly deceptive comments* at the Nobel Prize Lecture."
6	"The strategy of Muller and Stern to *deceive and obfuscate* on the nature of the dose response in the low dose zone was successful."
7	"Various leaders in the field repeated false limitations of the Caspari study (Higgins, 1951; Jolly, 2004; Singleton, 1954) that were inspired by the *deceptive* comments of Stern and Muller."
8	"…findings may be understood within the context of his *ideological* focus on establishing the LNT model for risk assessment and in the preservation of his legacy – a legacy that would have been severely tarnished if the *deceptive remarks* he made during his Nobel Prize Lecture had been discovered."
9	"These actions of *fabrication and falsification* by the Genetics Panel were undertaken to ensure that…"
10	"Following its acts of *falsification and fabrication* of the research record, the Genetics Panel continued to show its *arrogance* in the aftermath of the BEAR I Panel …."
11	"Thus, the President of the NAS was *complicit* in the decision not to require the BEAR Genetics Panel to document its support of the LNT model."
12	"The *dishonesty* of the Panel was nothing new as it was simply carrying on a tradition seeded a decade earlier by Hermann J. Muller at his Nobel Prize Lecture."
13	"The explicit *deceptions* of some Panel members continued even some 35 years after the fact"
14	"..Glass bears *false witness*. Glass's *most significant fabrication* is that …."
15	"The consensus story was not real but faked by Weaver and the Panel"
16	"In the selection of panel members, *one suspects* that Bronk and Weaver may have intended to *"stack the deck"* with radiation geneticists who supported the LNT.

A panel of scientists at a workshop organized by WHO, made up of a majority of continental Europeans, came to similar conclusions as the BEAR I genetics panel (WHO, 1957).

> "This Group takes note of the report of the National Academy of Sciences of the United States of America and that of the Medical Research Council of Great Britain.- … the Group notes the substantial similarity of the findings and recommendations of these reports and is in essential agreement with them" (WHO, 1957).

Whatever biases may or may not have existed in individual members of the BEAR I genetics panel, they would appear to have been washed away or balanced by the group process of debate and negotiation. The panel's report reflected a broader consensus by geneticists about the appropriateness of the LNT model for characterizing genetic risks in humans at low doses of ionizing radiation (Jolly, 2003).

Contemporary challenges to the LNT model for characterizing genetic risks in humans were made by physicians and physicists, rarely by geneticists (Jolly, 2003). In fact, geneticists tended to challenge those proposing a threshold model (Jolly, 2003). The concept of a single track of radiation causing damage to genes (i.e., the single-hit model) was a powerful theoretical concept. Unlike chemical exposures, no metabolization was required to cause damage. With fruit fly and emerging mouse data perceived to support the single-hit model, the 1956 genetics panel "immediately accepted the no-threshold principle for mutation production" while arguing with great intensity about how dangerous such mutations would, or would not be, to future generations (the so-called Classical/Balance controversy) (Beatty, 1987; Seltzer, 2007). In effect, they argued about the slope of a linear term, not the existence of a threshold.

Professor Calabrese tries to draw a number of inferences from transcripts of committee discussions and correspondence among panel members that he located from archives or were quoted in dissertations. Today, NAS staff members at public meetings caution attendees to focus on the final recommendations and conclusions, not on comments made by individual members of NAS committees during meetings. Committee members often ask questions or make comments that do not necessarily indicate their positions on particular subjects; they may change their minds on particular issues during the course of debate; and they often end up negotiating report language to produce a document they can all agree to. Responses to the charges made by Professors Calabrese concerning the BEAR I genetics panel have been published elsewhere by the current president of NAS and other NAS staff members (Cicerone and Crowley, 2014; Crowley et al., 2015).

3. Views on genetic risk estimates by subsequent NAS committees

How well have the judgments made by the 1956–1957 panels held up over time, now that very good datasets concerning the effects of ionizing radiation on large numbers of humans are available? For the LNT model, rather well. NAS panels have never doubted linearity of radiation induced genetic mutations, although they have accepted the data-driven idea of a slope that is reduced at low dose rates. As for cancer induction, successive NAS BEIR committees (NAS, 1972, 1990, 2006; Reissland, 1981) have become increasingly supportive of the LNT model, first treating the LNT model for cancer as a conservative approach for characterizing risks for radiation protection purposes, and today treating it as the best biologic model for characterizing both solid cancer and genetic risks in humans.

Estimates of genetic risk can also be compared to judgments made in later NAS reports. The 1956 Committee reported two separate estimates of risk, one for the first generation of offspring based on the estimated "doubling dose," and the second estimate for cumulative damage out to many generations. (Doubling dose is the amount of ionizing radiation given generation after generation that produces as many gene mutations that arise spontaneously.) Based on a comparison with the 2006 NAS BEIR (Biological Effects of Ionizing Radiation) VII report, the BEAR I genetics panel did well on its assessment of the mutation doubling dose. The range of doubling dose presented by the BEAR I genetics panel, 5–150 r, includes the value recommended by the BEIR VII committee (NAS, 2006), 1 Gy (approximately 100 r), which is a good result for a prediction made more than 50 years ago. The panel's estimate of the fraction of detrimental impacts seen in the *first* generation after a radiation dose is also roughly in agreement (within a factor of approximately 2) compared to later estimates (see Table 2).

The estimate made by six members of the BEAR I genetics panel for cumulative number of mutations over many generations from a single radiation exposure, the calculation that caused the greatest disagreement within the panel, was not estimated in later reports, because the gene-counting methods used were thought difficult to translate usefully into societal cost and human suffering (NAS,

Table 2
Comparison of risk metrics for radiation induced genetic damage that were made in 1956, 1990, and 2006 by panels of the (US) National Academy of Sciences.

Damage metric	1956 NAS (BEAR I)[a]	1990 NAS (BEIR V)[b]	2006 NAS (BEIR VII)[c]
Threshold	0	0	0
Doubling dose	50 (5–150)[d,e]	1	1
Original value			
Units	Roentgen (r)	Gy	Gy
Approximate value in 1956 dose units (r)	50 (5–150)	100	100
Damage from single 10 r dose in first generation			
Original Value	50,000[f]	6–35	3000–4700
Units	10^8 offspring	Extra cases per 10^6 liveborn offspring per rem	Risk per Gy per 10^6 Progeny
Value matching BEAR-1 dose and number of offspring	50,000	6000–35,000[g]	30,000–47,000
Total number of mutations passed on from single 10 r dose	5,000,000[h]	No estimate	No estimate

[a] NAS 1956, pp. 24–26.
[b] Table 2–1 in NAS 1990.
[c] Table 4–6 in NAS 2006.
[d] "Thus various arguments reduce the 5–150 r range, and several experienced geneticists have recently made estimates in the narrower range of 30–80 r".
[e] I have taken, 50 r, as the middle of the range for this comparison.
[f] Tangible inherited defects.
[g] Excluding congenital abnormalities, which in worst case was 10,000.
[h] Estimate by 6 panel members, only. A number of geneticists on the 1956 genetics panel did not think this to be a meaningful calculation, for the same reason that subsequent panels gave, namely that the numbers are not easily translated into societal cost and human suffering (NAS, 1956, p. 26).

1990). Thus, later NAS panels agreed with those members of the 1956 genetics panel that thought that.

> "…this kind of estimate is not a meaningful one to certain geneticists. Their principal reservation is doubtless a feeling that, hard as it is to estimate numbers of mutants, it is much harder still, at the present state of knowledge, to translate this over into a recognizable statement of harm to individual persons." (NAS, 1956), p. 26.

In the absence of later, more realistic, calculations with which to compare, it is not possible to tell if the +/− factor of ten uncertainty assigned to the 1956 estimate would bracket results from later models. Still, the 1956 BEIR I genetics panel got at least three out of four of its quantitative calculations reasonably consistent with current estimates made by subsequent NAS committees, namely the dose threshold (zero), the doubling dose, and the estimate of damage in the first generation resulting from a single exposure.

Professor Calabrese complains in his article that the true uncertainty in the cumulative population damage estimates was greater than a factor of ± 10. I agree with him, preferring ± 30, which is a value consistent with his calculation. I agree because the full uncertainty in the panel's estimate was only obliquely noted in the report, referred to as "widely different extreme ranges" with no quantification presented. Nevertheless, deciding on how to present scientific uncertainty to a lay audience is always a balancing act, and different groups may choose different solutions. However, a perceived weakness in the presentation of uncertainty is not sufficient grounds to condemn the entire report. In any case, Professor Calabrese's complaint about the BEAR I multi-generation mutation estimate is largely moot: 1) the published estimate was presented tentatively and with dissent noted, 2) it does not appear to have had much influence on subsequent research or radiation protection policies, and 3) the estimate was not used in developing the recommendations of the panel.

> "…in the end the numerical recommendation was based almost entirely on the amount of background radiation. Genetic calculations had little influence." (Crow, 1989).

I have seen nothing in the literature I cite, or anywhere else, that suggests that the published damage estimate (or the doubling dose estimate for that matter) had any effect on public policy or public opinion. For instance, these estimates were not reported in the news story about the BEAR-I report that appeared in the New York Times on the day of publication; the Times article focused its attention on the absence of a risk threshold by the genetics panel and the statement of life shortening made by a different panel (pathology panel) (New York Times, 6/13/1956). The entire BEAR I report, though, was printed in the newspaper.

The reports of the panel were particularly newsworthy and influential in affecting public opinion because they appeared to contradict the position of the US Atomic Energy Commission (USAEC) that there were no health issues associated with radiation fallout and possibly that there would be a hormesis effect (Creager, 2015; Hamblin, 2007; Seltzer, 2007). The prospects for high media attention were determined from the beginning of deliberations of the BEAR I panel because its members immediately agreed that the LNT model was appropriate for low dose radiation exposures and moved on to other issues.

4. Impact of BEAR I on subsequent NAS reports

In addition to saying that the BEAR report was corrupt and biased, the Calabrese article charges, without documentation, that successive NAS panels were duped into following the 1956 BEAR-I report's conclusions regarding the LNT model. Having myself served on nine NAS committees and experienced the vigorous debate process that is characteristic of these bodies, I find it difficult to imagine that any NAS committee would march in lock step with a previous committee, let alone one from 1956. Most likely, the five decades of data acquired after the BEAR-I report was published, including data from mice (Dubrova et al., 1998; Russell and Kelly, 1982), A-bomb survivors (Neel and Schull, 1991), and Chernobyl families (Dubrova, 2003), were more influential in determining the opinions of subsequent NAS BEIR committees, including the most recent BEIR VII committee (NAS, 2006), which presents some 500 pages of data and supporting analyses to

support its conclusions.

Furthermore, NAS committees began distancing themselves from some of the estimates in the BEAR-I report by 1972. The 1972 BEIR committee (NAS, 1972), asked to conduct a fresh look at radiation effects, noted that knowledge of genetics had been revolutionized since the BEAR I report was published. Studies of mutations in male mice showed no evidence of a dose threshold (Russell, 1965). The 1972 NAS Committee concluded that the genetic risks estimates in 1956 were "probably on the high and therefore conservative side," but there were far too many uncertainties to be dogmatic.

So, the high historical estimates of such great concern to Professor Calabrese today had already been addressed by NAS Committees more than forty years earlier. As for the LNT model, the 1972 committee had its own views and saw the model as a conservative and practical approach:

> "…the use of a non-linear hypothesis for estimating risks in support of public policy on radiation protection would be impractical in the present state of knowledge, since it would require consideration of individual variations in temporal and spatial distribution of tissue dose, as well as allowance for other variables which cannot be analyzed at this time."

Professor Calabrese has challenged the validity of certain articles about x-ray induced mutations in fruit flies published before 1956 on which the BEAR-I report relied. He claimed that there was data suggesting a dose-response threshold (see Appendix for a counterview). The 1972 BEIR panel was aware of this possibility:

> "Some Drosophila [fruit fly] data suggest a threshold, but there is good evidence that at least some of the effect has linear relationship to dose."

But, putting aside for the moment whether or not Drosophila data is relevant to current thinking about linearity, was the 1956 BEAR-I panel wrong or right about the fruit fly data as seen from today's fruit fly studies? It is apparently still a difficult question to resolve, as even today the cautionary statement by the 1972 panel seems appropriate. Some modern fruit fly studies show linearity down to doses 50 times lower than those used in fruit fly studies of the BEAR-I period and low enough to match doses of concern for routine radiation protection (Schweizer, 1995); yet some show threshold-like effects at much higher doses, such as a series of studies carried out by a research arm of the Japanese Electric Power Industry (Koana et al., 2012). (In the 2012 Koana study, some endpoints showed a U-shaped dose response (e.g., for so-called, small spots of mutant cells on Drosophila wings), but others showed linearity (e.g. for large spots).).

Fruit fly data are no longer used for estimates in NAS reports. The 1972 BEIR Committee relied primarily on mouse and human data for its risk estimates for genetic diseases. Also, the 1972 BEIR committee and its successors concluded that somatic (e.g. cancer) risks were more important for radiation protection than genetic risks, reducing the importance of any type of genetic data in radiation protection. Therefore, any debate about the strengths and limitations of the fruit fly studies used by the 1956 BEAR I panel, which makes up a good part of Professor Calabrese's article, is not relevant to 1972 and later NAS BEIR reports.

The 1990 NAS BEIR committee was the first to base its estimates solely on human data. It had the following comments about the BEAR-I genetics panel:

> "The doubling dose range given by the BEAR Committee would now be considered to apply to acute radiation. It must be remembered that at the time that the BEAR report was written, neither the dose-rate effect nor the distinction between premeiotic and postmeiotic cell stage response to radiation were known."

The latest NAS report, BEIR VII (2006), was also dismissive of the 1956 BEAR I report, saying that its quantitative estimates were "nothing more than educated guesses." Thus, once again, Professor Calabrese's claim that successive panels followed the BEAR-I report is not validated.

The NAS (2006) BEIR VII report concluded, based on then-current data and understanding of radiation biology, that the dose-response model for cancer was linear at low doses:

> "A comprehensive review of the biology data led the committee to conclude that the risk would continue in a linear fashion at lower doses without a threshold and that the smallest dose has the potential to cause a small increase in risk to humans."

The 2006 BEIR VII report notes that a dose-rate effectiveness factor (DREF) of 3 has been used in post-1970 NAS BEIR reports to extrapolate downward high *dose-rate* mouse genetic mutation data to low *dose-rates* for genetic mutations. (In contrast, the BEIR VII report recommended a DREF of 1.5 for solid cancer). Although subsequent panels of the NAS have downgraded the magnitude of genetic risks, they have steadily increased the LNT slope for cancer effects.

The 2006 NAS BEIR VII report devotes a chapter to radiation hormesis, the model championed by Professor Calabrese. In fact, Professor Calabrese is listed as having made a presentation to the BEIR VII Committee, but his arguments for hormesis were not adopted. Furthermore, the 2006 BEIR VII committee considered models other than hormesis, including supralinearity, which posits that radiation induced genomic instability and bystander effects increase cancer risks at low doses relative to the LNT model (Morgan and Sowa, 2009). In its analysis, the 2006, NAS Committee (BEIR VII) considered all the studies available at the time that Calabrese and other hormesis supporters were convinced invalidated the LNT, as well as studies supporting the antithetical view, namely, supralinearity. The committee, which consisted of 17 experts from universities and research institutions, found that the bulk of the available studies and biological reasoning supported the LNT model. I note that the committee's draft report was reviewed by yet another 16 experts.

Supporters of hormesis claim that studies since 2005 have changed the situation. So, too, do supporters of the LNT, but they claim the change is in favor of the LNT. They point to the post-2006 epidemiological studies on cancer incidence and mortality. These include the latest results from A-bomb survivor studies as well as studies on over 600,000 radiation workers. For a listing and discussion of these studies, see (Beyea, 2012). Risk estimates from these post-2005 studies are consistent with or higher than previous studies. For example, the most recent worker study (Leuraud et al., 2015), with ~300,000 subjects, reported direct estimates of a linear risk per unit of protracted dose for blood cancers in ranges "typical of environmental, diagnostic medical, and occupational exposure.".

5. LNT and radiation protection

The impact of the BEAR I report on the subsequent adoption of the LNT model for radiation protection should not be overstated. Ron Kathren, no friend of the LNT model,, attributed the introduction of this model to a 1954 Report (No. 17) by the National Council on Radiation Protection (NCRP), followed by a similar proposal by the British in 1955 (Kathren, 1996):

> "In place of the tolerance dose, Report No. 17 introduced the concept of the maximum permissible dose (MPD). Implicit in

the MPD was the idea of acceptable risk, and hence a non-threshold model, the basis for which were the observations of linearity in genetic mutations in *Drosophila melanogaster* which, for protection purposes, were assumed to also apply to somatic mutations."

The BEAR-I report was issued two years after NCRP report 17 was published. Report 17 used the same starting assumptions challenged by Professor Calabrese as biased and corrupted. Kathren does not even mention the BEAR I report, let alone suggest it played any significant role in developing or maintaining the new paradigm of linearity. Given the NCRP's role in advising the US government on radiation protection standards, it seems quite likely that the LNT model would have been adopted for radiation protection purposes in the United States even if BEAR I had never been published.

On the other hand, BEAR-I did have a role, along with the International Commission on Radiation Protection and the NCRP, in reducing limits on worker exposure to radiation (Taylor, 1957), limits that still hold today. The acceptance of the LNT model for radiation protection did not bar radiation exposure for workers or members of the public. The BEAR-I report also influenced the politics of the time, elevating public concerns about radioactive fallout from nuclear weapons testing, thus helping to bring about the adoption of the atmospheric test ban treaty. The BEAR I report also heightened fears about ionizing radiation exposure regardless of its magnitude (Crow, 1987; Crow, 1995). Contrasted with the USAEC's denial of any effect, the BEAR I report apparently increased public suspicion of government on radiation issues (Creager, 2015; Hamblin, 2007).

What is often lost in disputes over radiation dose response models is that risks at the low dose levels that are being debated are also low, whether assessed using a linear, supralinear, or threshold model. That means large differences in risk estimates can be expected in study results, including contradictory differences, particularly when sample sizes are small. Human radiation biology is not physics; experiments cannot ethically be done on people. Scientists must rely on non-human data, for example biomarkers of debatable importance in cells irradiated *in vitro*, and/or "opportunistic" exposure situations where individual exposures and their uncertainties may only be roughly known. Furthermore, human health outcomes of interest (e.g., cancer) arise long after a radiation exposure is received, increasing the number of variables that can modify causation. And such health outcomes can have a number of other contributors besides radiation, reducing the "signal to noise" ratio, as the radiation dose declines. As a result of such limitations, there is some evidence that can be found in some studies for virtually any dose-response function at low doses.

Expert committees established by scientific organizations like the NAS, usually at the request of government agencies or legislatures, are charged with weighing all available evidence in addressing their study mandates, including contradictory evidence, which they do in detail. Weighing evidence requires subjective judgments, so committee reports are unlikely to please every scientific constituency.

Moreover, different committees can reach different conclusions. For example, a 2005 French Academy of Sciences/National Academy of Medicine report was skeptical of the LNT model for radiation protection against cancer, particularly, when it came to balancing risks from diagnostic radiation exposures against the medical risks of avoiding diagnostic testing (Tubiana, 2005).

The process used by NAS committees to weigh the relevant evidence and develop consensus reports through discussion and negotiation contrasts with approaches taken by partisans of various theories; they tend to assess studies that agree with their views by the study's strengths and assess studies that disagree with them by the study's weaknesses. Scientific partisans have an important role to play in science by challenging prevailing views, but not by launching character attacks.

A new NAS panel on the biological effects of radiation is in the planning stage (http://dels.nas.edu/), so advocates of hormesis and other models can expect to have another opportunity to make their cases in the not-too-distant future. For the moment, when an attempt is made to quantify risks in a low dose range, all views on dose response can be incorporated by taking a linear response as the centroid, with uncertainty bands broadened to incorporate the theories of both hormesis and supralinearity (Beyea, 2012).

Appendix

1) Did the BEAR-I panel bias its views to gain funding for individual's research, as Dr. Calabrese charges? The main argument against this claim is given in the text, namely that the report was not biased in the first place. But the charge is also invalid when it comes to the details on which the inference was based, for the charge is based on an unrepresentative sample from the historical record and it ignores the context of the times. I have never been on a panel of scientists who didn't think that more research was a social good. That does not translate into corruption. Furthermore, the disparaging quotes from Dobzhansky and Demeric used in the article, which contained talk of bending views to increase research dollars, were made a year after the BEAR-I report was published, making them of questionable relevance. And Dobzhansky did not even serve on the first BEAR panel, only the second one. In addition, the quotes cited in Calabrese came from one faction in the debate, namely those who supported low risk numbers, not from panel members like Muller and others who supported high risk numbers.

It should also be noted that the research fund being discussed in the correspondence was a proposal of one of the correspondents, namely Demeric, who wrote that he thought more research was necessary before geneticists should give risk estimates (Seltzer, 2007), p 305. He worried that traditional funding would lead to a dissipation of effort. It was Dobzhansky, Muller's main scientific antagonist, who wrote about a willingness to bend his views a bit. In contrast to Dobzhansky, Jolly argues that Muller was concerned in the debate about the effect on the public and policy debates over radiation exposure, not funding (Jolly, 2003), p 305. Moreover, it was Dobzhansky who was charged at the time to have "bent [his] interpretation of experimental results to get money out of the AEC [U.S Atomic Energy Commission]." (Lewontin et al., 2001; Seltzer, 2007, p 450). (Readers should be skeptical of all such mutterings about the ethics of scientific competitors, whether expressed in the past or today.).

To provide additional balance to Professor Calabrese's analysis, it is only necessary to go to his main published sources for negative quotations about the 1956 panel, which include fascinating Ph.D. theses by Michael Seltzer and J. Christorpher Jolly, as well as an equally fascinating article by historian Jacob Hamblin. Most radiation genetics work, including that of a number of BEAR-I panelists, was funded by the US Atomic Energy Commission (USAEC), which was not objective about the results it wanted to see, according to Seltzer and Hamblin, and was not adverse to promoting a "hormesis-like" model.

> "…with the public controversy over radiation hazards, it became the undeviating goal of the AEC to justify scientifically the position that fallout and low levels of radiation pose no threat to humans, and might even be beneficial genetically." (Seltzer, 2007) p. 290.

H.J. Muller, the main villain in the Calabrese analysis, was a nuisance to the USAEC. Seltzer and other sources (Beatty, 1987; Hamblin, 2007) indicate that in 1955, the USAEC blocked Muller from giving a paper on the genetic hazards of radiation at the United Nations International Conference on the Peaceful Use of Atomic Energy held in Geneva. Muller nevertheless was able to attend as an observer and received a standing ovation, according to a contemporary (Hamblin, 2007).

Seltzer goes on to state that, in general, the USAEC "…sought to dominate all the relevant committees, government and independent, that were formed to study and/or recommend policy on radiation exposure limits.".

In a similar vein, Hamblin argues that this attempt to dominate committees extended to the BEAR-I panel; he claims that the panel was not truly independent of the USAEC, with USAEC scientists on many panels and subpanels and holding the keys to much important data. In direct contradiction to Calabrese's claims about the direction of NAS bias, Hamblin argues that the NAS staff was too solicitous of the USAEC; that the staff allowed the USAEC to negotiate with the panel about content (e.g. commenting on drafts). However, Hamblin still had praise for the report itself:

> "This is not to say that the BEAR report itself was a whitewash; quite the contrary, it was scientific negotiation at its most successful. For a brief moment, it balanced the goals and expectations of a host of interests. But the results of the report were used repeatedly by the USAEC and the Eisenhower administration to play down the risks of fallout by calling them minute additions to the bath of natural radiation in which humans already lived."

Thus, from my reading of the Seltzer dissertation, the Jolly dissertation and the historical analysis of Hamblin, a different picture emerges than the one Calabrese paints. Anyone at the time who took a view opposite to the USAEC on fallout risk was potentially vulnerable to loss of funding or loss of future opportunity of funding. And, the USAEC would have appeared to have been watching, given the USAEC-friendly scientists on the genetics panel, including Shields Warren, the former head of the USAEC's Division of Biology and Medicine (1948–1952), who had "authored the USAEC's basic assumptions" (Hamblin, 2007). From this broader viewpoint the panel exhibited courage in my view when it deviated from the USAEC party line by insisting that the potential genetic risks of radiation exposure had to be stressed in the report.

In an unpublished project report (Beyea, 2016), I have offered responses to criticisms of historical figures by Professor Calabrese not covered here that I deem unfair, but which have minor relevance to the key issues under debate. I do so because a defense of these individuals (including, Bentley Glass, Warren Weaver, James Crow, Hermann Muller, and Detlev Bronk) is warranted in face of the prosecutorial case made in the Calabrese article.

2) Did political considerations lead to a biased BEAR-I report? Once again, the BEAR-I report was not biased when compared to other reviews in that period. Nevertheless, when NAS panels are given controversial topics, it is impossible for political implications to be completely avoided, which is one reason that negotiations over language can get heated and can be time consuming; it is also one reason why the NAS tries to bring balance to committees through the appointment process. Like most NAS committees, a wide range of scientific viewpoints, including scientific-political viewpoints, was represented among the 16 members of the BEAR-I genetics committee, leading to extensive disputes before a consensus was reached (Beatty, 1987; Beatty, 2006; Crow, 1995; Jolly, 2003). Obtaining agreement required compromise and the inclusion of multiple points of view in the final document. However, not all points of scientific view can be included in NAS committees to keep their sizes workable. The idea of effects going to zero at a finite dose for *genetic* effects (Calabrese's claim) was not a debate of the day. The absence of a threshold was a widely accepted view in the genetics community at the time for genetic (but not necessarily somatic) effects (Jolly, 2003; Kathren, 1996); the big debate at the time was whether all mutations induced by fallout radiation would have a negative effect on the genetic makeup (as Muller and supporters argued) or whether increased variance could significantly moderate the damage component (as Dobzhansky and his supporters argued) (Crow, 1987; Hamblin, 2007; Seltzer, 2007). Calabrese may think from his present-day vantage point that the 1956 BEAR I panel was debating the wrong question, but, with the exception of Ralph Singleton, who studied corn, there was little concern about the validity of the LNT model among geneticists of the era, and even Singleton had muted his concern by late 1955 based on his evolving studies (Jolly, 2003; Konzak and Singleton, 1956). (Singleton served on the 1956 BEAR I agriculture panel, which assessed the impact on food supplies of nuclear weapons fallout.)

Later NAS committees would take on the question of the validity of the LNT model. In fact, for the 1980 report, consensus broke down and two minority reports were prepared, one suggesting pure linearity for cancer, one supporting a pure quadratic dose response (Marshall, 1979). The remainder of the committee supported a mid-view, namely a linear-quadratic response, which was linear at the lowest doses, but with a reduced slope. Subsequent committees went back to the linear cancer model, based on the evolving data situation.

At the BEAR-I genetics panel meetings, the debate was not about linearity; it was about the strength of the association. Both sides were represented, with Sewall Wright and others as surrogates for Dobzhansky. Both positions were represented in the final document to prevent a break down in consensus (Crow, 1995). I note that, although Dobzhansky was not able to serve on the first panel, he did find time to serve on the second BEAR panel (NAS, 1960), which supported the recommendations of the first panel. Nevertheless, had Dobzhansky been able to participate in the 1956 panel, based on my experience with such panels, I expect that the report's text would have had further explication of his views than were actually incorporated.

Both Dozbransky and Muller were aware of political implications of their ideas, according to historian, John Beatty:

> "Dobzhansky and Muller both appealed to the dangers of misguided social policy that might have resulted from prematurely resolving their controversy in the other's favor. They called for high empirical standards on those grounds, more than once seeking to forestall the resolution of their dispute in this way." (Beatty, 1987).

In casting aspersions about Muller's politics, Professor Calabrese does not give an objective picture of Muller, a brilliant but complex figure (Beatty, 1987; Crow, 1995; Crow, 2005; Paul, 1988). According to these authors Muller was concerned about the effects of fallout on the gene pool, but he supported the US having nuclear weapons and was initially wary of an atmospheric test ban because he was more afraid of the Soviet Union than nuclear weapons. He also was a supporter of eugenics. Dobzhansky, too, was complex and a larger-than-life figure in biology. Like most scientists, Muller and Dobzhansky had their personal strengths and weaknesses.

3) Were key scientific papers by Curt Stern and collaborators fraudulent and did Stern try to deceive the scientific community?.

The idea that a man like Stern (see Neel (1983) for an appreciation) would deliberately deceive the scientific community leaves me dumbstruck. Nevertheless, Professor Calabrese has

apparently come to believe that key papers by Curt Stern and collaborators (Caspari and Stern, 1948; Spencer and Stern, 1948; Uphoff and Stern, 1949) were influenced by Muller and dishonestly presented. Calabrese's work has spawned similar criticisms of this pre-1960 Drosophila (fruit fly) data (Siegel et al., 2016). Based on his review of correspondence, Calabrese concluded that the paper by Caspari and Stern was the best of the lot and the rest should have been discounted as flawed. In contrast, Stern saw to it that all three papers were published. Dr. Calabrese stated that the Caspari paper supported a threshold dose response, which is incorrect. The paper was a test of dose-rate independence; there was no questioning of linearity for one-time exposures. The paper was a test of the single-hit theory.

> "If the result turns out to be correct, it would necessitate a revision of the classical hit theory of induction of mutations." (Uphoff and Stern, 1949).

Three possible revisions to the classical theory are listed in the paper, only one of which is a dose-rate threshold response. The other two are 1) a multi-hit model, and 2) a repair model. A repair model might be closest to the current practice of using a dose-rate effectiveness factor (DREF) for low-dose exposures, or, perhaps a fourth category should have been added. In the summary paper by Uphoff and Stern, published in *Science*, which analyzed all three data sets, the authors state.

> "Viewing all experiments together, it appears that irradiation at low dosages, administered at low intensity, induces mutations in Drosophila sperm. There is no threshold below which radiation fails to induce mutations."

Unlike, Professor Calabrese, upon reviewing the paper, I found the interpretation reasonable, as the *Science* reviewers must have. All three data sets show an increase over controls, although the data set preferred by Professor Calabrese shows a high p-value (0.29), but that does not mean the effect was zero. Looking at the effects value for all three studies, the combined data suggest to me, and apparently to Caspari and Stern and the Science reviewers, that it was not necessary to invoke any of the three proposed alternatives to the single-hit theory. Possibly, invoking a DREF, which later became the norm, would have improved the comparison of the three studies.

Based on my review of Professor Calabrese's objectivity as a historical analyst of matters related to thresholds, and given the fact that the Stern papers take up 20 linear feet in the archives of the American Philosophical Society, I am skeptical of his claim that a full reading of the Stern/Muller correspondence reveals that they allowed any of the papers to be published knowing there was a fatal flaw. All papers, of course, have weaknesses, which are usually discussed within research groups before publication. Not all of the discussion appears in correspondence; some of it occurs in face-to-face and telephone conversations. In any case, it would be helpful if Professor Calabrese would put up on the web the correspondence that he collected, as well as the correspondence he cited, so that others could make their own judgments about the serious attacks he has made to the reputations of major figures in radiation biology.

Professor Calabrese speculates that the lead author for the Caspari and Stern paper must have been unhappy with the resolution proposed in the summary paper in *Science*. Yet in 1979, Caspari professed pride in the three papers that Calabrese discusses, including the two that Calabrese denigrates, saying that this work formed "the basis of our present knowledge of mutagenic radiation effects.(Seltzer, 2007), footnote 211 p. 286." In any case, these three papers were published years before the BEAR I report, so they were neither the responsibility of the BEAR-I genetics panel nor NAS. And another paper supportive of dose-rate independence was published before the panel finished its work (Luning et al., 1955).

In conclusion, the historical record is so rich and complicated that it can support multiple competing narratives depending, for instance, on how extreme a filter is applied to it, the agenda that the filtering is meant to serve, and how conspiratorial the analyst wants to get, especially if use is made of inferences about motives. Humans are complex, with multiple motives, known and unknown, which influence their decisions. Once motives are fair game, where does it stop? What about the motives of Muller's competitors, e.g., Dobzhansky and Wright? What about the motives of analysts, such as Seltzer, Hamblim, Calabrese, and myself? There is no scientific way to unravel motives and their influence. Let such discussions occur in history and political science journals, where readers and reviewers are versed in the methods of historical analysis.

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